



Complete Summary

GUIDELINE TITLE

Antithrombotic therapy for peripheral artery occlusive disease. American College of Chest Physicians evidence-based clinical practice guidelines (8th edition).

BIBLIOGRAPHIC SOURCE(S)

Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):815S-43S. [208 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Clagett GP, Sobel M, Jackson MR, Lip GY, Tangelder M, Verhaeghe R. Antithrombotic therapy in peripheral arterial occlusive disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):609S-26S.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [December 3, 2008, Innohep \(tinzaparin\)](#): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.
- [February 28, 2008, Heparin Sodium Injection](#): The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with

symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.

COMPLETE SUMMARY CONTENT

**** REGULATORY ALERT ****

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Peripheral arterial occlusive disease, including:

- Chronic limb ischemia
- Acute limb ischemia

GUIDELINE CATEGORY

Management

Prevention

Treatment

CLINICAL SPECIALTY

Cardiology

Emergency Medicine

Family Practice

Internal Medicine

Surgery

INTENDED USERS

Advanced Practice Nurses

Allied Health Personnel

Health Care Providers

Nurses

Patients

Physicians

Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To provide evidence-based recommendations on the use of antithrombotic therapy in patients with peripheral arterial occlusive disease
- To update evidence-based recommendations for the use of antithrombotic and thrombolytic therapy for the management of thromboembolic conditions

TARGET POPULATION

- Patients with acute or chronic peripheral arterial occlusive disease (PAOD)
- Patients requiring vascular grafts
- Patients requiring carotid endarterectomy
- Nonoperative patients with asymptomatic carotid stenosis (primary or recurrent)
- Patients undergoing lower extremity endovascular procedures (i.e., balloon angioplasty with or without stenting)

INTERVENTIONS AND PRACTICES CONSIDERED

Management

Chronic Limb Ischemia and Intermittent Claudication

1. Lifelong antiplatelet therapy
2. Aspirin
3. Clopidogrel
4. Ticlopidine
5. Cilostazol

The use of anticoagulants, pentoxifylline, and prostaglandins was considered but not recommended.

Acute Arterial Emboli or Thrombosis

1. Long-term anticoagulation with vitamin K antagonist (VKA) following systemic anticoagulation with unfractionated heparin (UFH)
2. Intra-arterial thrombolytic therapy

Vascular Reconstructive Surgery

1. Intravenous (IV) UFH
2. Aspirin
3. Aspirin in combination with VKAs (for those at high risk only)

The use of preoperative dextran, heparin, or long-term anticoagulation with VKAs for all extremity reconstructions was considered but not recommended.

Carotid Endarterectomy, Nonoperative Patients with Asymptomatic Carotid Stenosis, Lower-extremity Balloon Angioplasty (With or Without Stenting)

Aspirin therapy

Dual antiplatelet therapy and anticoagulation with heparin or VKA was considered but not recommended.

MAJOR OUTCOMES CONSIDERED

Effectiveness and safety of treatment as evidenced by the following:

- Rates of surgical intervention required for treatment
- Cardiovascular morbidity and mortality
- Rates of ongoing or recurrent ischemia
- Patency of vein grafts

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Process of Searching for Evidence

Defining the clinical question provided the framework for formulating eligibility criteria that guided the search for relevant evidence. In specifying eligibility criteria, authors identified not only patients, interventions, and outcomes, but also methodologic criteria. For many recommendations, authors restricted eligibility to randomized controlled trials (RCTs).

For many questions, randomized trials did not provide sufficient data, and chapter authors included observational studies when randomized trials were not the most appropriate design to address the research question. In particular, randomized trials are not necessarily the best design to understand risk groups, that is, the baseline or expected risk of a given event for certain subpopulations. Because no interventions are typically examined in questions about prognosis, one replaces interventions by the duration of exposure measured in time.

Identifying the Evidence

To identify the relevant evidence, a team of librarians and research associates at the McMaster University Evidence based practice center (EPC) conducted comprehensive literature searches. Methodologic experts (including the editors) and the EPC librarians reviewed each question to ensure the development of a comprehensive search strategy. For example, for questions about antiplatelet agents, the EPC consulted chapter authors to ensure that the search included all

relevant antiplatelet agents. More specifically, authors then decided whether to include dipyridamole in a search that already included aspirin, clopidogrel, and ticlopidine.

For each question the authors provided, the librarians searched the Cochrane Database of Systematic Reviews, MEDLINE, and Embase for published English-language literature and human studies between 2002 and May 2006. To filter MEDLINE and Embase search results for RCT evidence, the librarians used the search strategy developed by the Cochrane Collaboration. These searches updated the more comprehensive and sensitive searches conducted for the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy: Evidence Based Guidelines.

The EPC team conducted separate searches for systematic reviews; RCTs; and, if applicable, observational studies. For observational studies, searches were not restricted in terms of methodology. Although increasing the probability of identifying all published studies, this sensitive approach resulted in large numbers of citations for many of the defined clinical questions. Therefore, trained research assistants screened the citation list developed from the search using criteria of increased specificity to reduce the number of irrelevant citations that the authors received. These irrelevant citations included press news, editorials, narrative reviews, single-case reports, studies that included fewer participants than specified by authors as an inclusion criterion, animal studies (any nonhuman studies), and letters to the editor. Authors did not include data from abstracts of meetings for the development of recommendations, and the guideline developers did not explicitly use Internet sources to search for research data. Authors were encouraged, however, to mention abstracts that reported on groundbreaking data that were particularly relevant to a specific question in the chapters in order to alert readers that new, fully published evidence might become available shortly.

Standard Consideration of Study Quality

High-quality clinical guidelines should pay careful attention to the methodologic quality of the studies that form the basis of their recommendations. Using the example of the prevention of venous thromboembolism during air travel, Table 1 in the methodology companion (see "Availability of Companion Documents" field) shows the criteria for assessment of study quality (randomization, concealment or treatment allocation, blinding, completeness of follow-up, and whether the analysis was performed according to the intention-to-treat principle), and Table 2 in the methodology companion (see "Availability of Companion Documents" field) shows the presentation of results that were circulated to the authors. Whereas all authors attended to these criteria, the guideline developers have summarized the results of the quality assessment for only a minority of the recommendations. Readers can find these summaries in an online appendix to the recommendations (see online supplemental data).

In assessing the quality of observational studies, the guideline developers did not make a distinction between prospective and retrospective because the key issues are unbiased sampling, high-quality measurement of patient characteristics and outcomes, and complete follow-up.

Although it is more likely that these quality criteria will be achieved in prospective studies, prospective studies may fail to achieve them, and retrospective studies may succeed. The guideline developers did make a key distinction about whether internal comparisons exist and their nature. Studies without internal comparisons received the label "case series" unless they met the following criteria: (1) a protocol existed before the date of commencement of data collection; (2) a definition of inclusion and exclusion criteria was available; (3) the study reported the number of excluded patients; (4) the study conducted a standardized follow-up, including description of schedule of follow-up, investigation of suspected outcomes, and criteria used to define outcomes; and (5) the study reported all losses to follow-up.

The guideline developers labeled studies that met these criteria "cohort studies without internal controls." Studies with internal comparisons received the label "cohort studies with concurrent controls" or "cohort studies with historical controls." These cohort studies may succeed or fail to ensure settings, similar time frames, adjustment for differences in patients' characteristics, and follow-up with patients. These features were captured in descriptive tables provided to authors when requested from the EPC.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodological quality of the underlying evidence (A, B, or C). See "Grades of recommendations for antithrombotic agents" in the "Availability of Companion Documents" field and the "Rating Scheme for the Strength of the Recommendations." field.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Summarizing Evidence

The electronic searches also included searches for systematic reviews. If authors were satisfied with a recent high-quality systematic review, evidence from that review provided a foundation for the relevant recommendation.

Pooled analyses from high-quality systematic reviews formed summary data on which panelists based their recommendations wherever possible. Pooling offers the advantage of obtaining more precise estimates of treatment effects and allows for greater generalizability of results. However, pooling also bears the risk of spurious generalization. In general, the summary estimates of interest were the different types of outcomes conveying benefits and downsides (risk, burden, and cost). When pooled estimates of effects were not available, the McMaster University Evidence based practice center (EPC) conducted metaanalysis to obtain pooled estimates for specific questions. These were questions that authors had specifically identified.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Group-Specific Recommendations

In general, the guideline developers have endeavored to make their recommendations as specific as possible for patient subgroups differing according to risk. Whenever valid prognostic data were available, the guideline developers used them to estimate absolute effects and made recommendations accordingly. Unfortunately, reliable prognostic indexes are not usually available, limiting the extent to which such group-specific recommendations are possible.

Acknowledge Values and Preferences and Resource Use Underlying Recommendations

Under ideal circumstances, knowledge of average patient values and preferences would be available for every recommendation, the panel members would summarize these values and preferences, and they would be integrated into the recommendations that guideline developers make. The guideline developers asked all chapter chairs before beginning the searches for the relevant literature to identify recommendations that they believed were particularly sensitive to patients' values and preferences. Moderate-quality evidence regarding values and preferences bearing directly on the recommendations proved available for only the chapter that addresses antithrombotic therapy in patients with atrial fibrillation. The panelists bore in mind what average patient values and preferences may be; the process, however, is speculative.

The guideline developer's main strategy for dealing with this unsatisfactory situation is to make the values and preferences underlying the recommendations explicit whenever the panelists believed that value and preference issues were crucial for a recommendation.

In addition, the guideline developers involved three consultants with expertise in the area of values and preferences to collaborate with the chairs of two chapters and try to ensure that the guidelines adequately represented the views of patients. This collaboration led to extensive discussions among the chapter

authors and the consultants and the reflection of these discussions in the associated values and preference statements.

Finalizing and Harmonizing Recommendations

After having completed the steps the guideline developers have described above, the guideline authors formulated draft recommendations before the conference, which laid the foundation for authors to work together and critique the recommendations. Figure 1 in the methodology companion (see "Availability of Companion Documents" field) shows the process of guideline development and review. Drafts of chapters that included draft recommendations were usually distributed for peer review to at least two panel members and were always reviewed by at least one panel editor before the conference. Written critiques were prepared and returned to the authors for revision of their work. At the plenary conference, a representative of each chapter presented potentially controversial issues in their recommendations. Chapter authors met to integrate feedback and consider related recommendations in other chapters and to revise their own guidelines accordingly. Authors continued this process after the conference until they reached agreement within their groups and with other author groups who provided critical feedback. The editors of this supplement harmonized the chapters and resolved remaining disagreements between chapters through facilitated discussion. All major correspondence and discussions at the meeting were recorded in written and audio protocols and are publicly available.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
		from observational studies	estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

COST ANALYSIS

For these guidelines, the guideline developers implemented recommendations of a recent American College of Chest Physicians (ACCP) task force on integrating resource allocation in clinical practice guidelines by restricting resource expenditure consideration to a small number of recommendations for which they were particularly relevant. The guideline developers relied on two consultants with expertise in economic assessment to help with the process of considering costs in those small numbers of recommendations that the guideline developers considered very important to the decision.

Recommendations highly sensitive to resource allocation now include value and preference statements regarding how cost issues were integrated.

Refer to "Strategies for incorporating resource allocation and economic considerations" (see "Availability of Companion Documents" field) for details of the cost analyses.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The American College of Chest Physicians (ACCP) Health Science Policy (HSP) established a process for the thorough review of all ACCP evidence-based clinical practice guidelines. After final review by the editors, the guidelines underwent review by appropriate NetWorks of the ACCP (for these guidelines, the Cardiovascular and Pulmonary Vascular NetWorks), the HSP, and the Board of Regents. The latter two have the right of approval or disapproval but usually work with the guideline authors and editors to make necessary revisions before final approval. Each group identified primary reviewers who read the full set of chapters as well as individual committee members who were responsible for reviewing one or more chapters. The reviewers considered both content and methodology as well as whether there was balanced, not biased, reporting and adherence to HSP processes. Finally, the *CHEST* editor-in-chief read and forwarded the manuscripts for nonbiased, independent, external peer review before acceptance for publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of recommendation (1A, 1B, 1C, 2A, 2B, 2C) are defined at the end of the "Major Recommendations" field.

Chronic Limb Ischemia and Intermittent Claudication

1. In peripheral artery disease (PAD) patients with clinically manifest coronary or cerebrovascular disease, the guideline developers recommend lifelong antiplatelet therapy in comparison to no antiplatelet therapy **(Grade 1A)**.
2. In those without clinically manifest coronary or cerebrovascular disease, the guideline developers suggest aspirin (75–100 mg/day) over clopidogrel **(Grade 2B)**. In patients who are aspirin intolerant, the guideline developers recommend clopidogrel over ticlopidine **(Grade 1B)**.

Underlying values and preferences: This recommendation places a relatively high value on avoiding large expenditures to achieve uncertain, small reductions in vascular events.

3. In patients with PAD and intermittent claudication, the guideline developers recommend against the use of anticoagulants to prevent vascular mortality or cardiovascular events **(Grade 1A)**.
4. For patients with moderate-to-severe disabling intermittent claudication who do not respond to exercise therapy, and who are not candidates for surgical or catheter-based intervention, the guideline developers recommend cilostazol **(Grade 1A)**. The guideline developers suggest that clinicians not use cilostazol in those with less disabling claudication **(Grade 2A)**. The guideline developers recommend against the use of pentoxifylline **(Grade 2B)**.

Underlying values and preferences: Because of the cost of cilostazol therapy, and the safety and efficacy of an exercise program, the guideline developers recommend cilostazol treatment be reserved for patients with moderate-to-severe claudication who have tried and failed an exercise program, and are not candidates for vascular surgical or endovascular procedures.

5. For patients with intermittent claudication, the guideline developers recommend against the use of anticoagulants **(Grade 1A)**.
6. For patients with limb ischemia, the guideline developers suggest clinicians do not use prostaglandins **(Grade 2B)**.

Acute Limb Ischemia

1. In patients who suffer from acute arterial emboli or thrombosis, the guideline developers recommend immediate systemic anticoagulation with UFH, over no anticoagulation **(Grade 1C)**. In patients undergoing embolectomy, the guideline developers suggest following systemic anticoagulation with UFH with long-term anticoagulation with VKA **(Grade 2C)**.
2. In patients with short-term (< 14 days) thrombotic or embolic disease, the guideline developers suggest intra-arterial thrombolytic therapy **(Grade 2B)**, provided patients are at low risk of myonecrosis and ischemic nerve damage developing during the time to achieve revascularization by this method.

Underlying values and preferences: This recommendation places relatively little value on small reductions in the need for surgical intervention and relatively high value on avoiding large expenditures and possible major hemorrhagic complications.

Vascular Bypass Grafts

1. For patients undergoing major vascular reconstructive procedures, the guideline developers recommend intravenous (IV) unfractionated heparin (UFH), prior to the application of vascular cross clamps **(Grade 1A)**.
2. For all patients undergoing infrainguinal arterial reconstruction, the guideline developers recommend aspirin (75–100 mg, begun preoperatively) **(Grade 1A)**. The guideline developers recommend against the routine use of perioperative dextran, heparin, or long-term anticoagulation with vitamin K antagonist (VKA) for all extremity reconstructions **(Grade 1B)**.
3. For patients receiving routine autogenous vein infrainguinal bypass, the guideline developers recommend aspirin (75–100 mg, begun preoperatively) **(Grade 1A)**. The guideline developers suggest that VKA not be used routinely in patients undergoing infrainguinal vein bypass **(Grade 2B)**. For those at high risk of bypass occlusion and limb loss, the guideline developers suggest VKA plus aspirin **(Grade 2B)**.

Underlying values and preferences: These recommendations place relatively little value on small increases in long-term patency that may be statistically uncertain, and a relatively high value on avoiding hemorrhagic complications.

4. For patients receiving routine prosthetic infrainguinal bypass, the guideline developers recommend aspirin (75–100 mg, begun preoperatively) **(Grade 1A)**. The guideline developers suggest that VKA not be used routinely in patients undergoing prosthetic infrainguinal bypass **(Grade 2A)**.

Underlying values and preferences: These recommendations place relatively little value on small increases in long-term patency that may be statistically uncertain, and a relatively high value on avoiding hemorrhagic complications.

Carotid Endarterectomy

In patients undergoing carotid endarterectomy, the guideline developers recommend that aspirin, 75–100 mg, be given preoperatively to prevent perioperative ischemic neurologic events. The guideline developers recommend lifelong postoperative aspirin (75–100 mg/day) **(Grade 1A)**.

Asymptomatic Carotid Stenosis

1. In nonoperative patients with asymptomatic carotid stenosis (primary or recurrent), the guideline developers recommend lifelong aspirin, 75–100 mg/d **(Grade 1C)**. In this patient group, the guideline developers recommend against dual antiplatelet therapy with aspirin and clopidogrel **(Grade 1B)**.
2. For patients undergoing lower-extremity balloon angioplasty (with or without stenting), the guideline developers recommend long-term aspirin (75–100 mg/day) **(Grade 1C)**. For patients undergoing lower-extremity balloon angioplasty (with or without stenting), the guideline developers recommend against anticoagulation with heparin or VKA **(Grade 1A)**.

Definitions:

Grading Recommendation

Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
Strong recommendation, high-quality evidence, Grade 1A	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate-quality evidence, Grade 1B	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies	Recommendation can apply to most patients in most circumstances; higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low or very low-quality evidence, Grade 1C	Desirable effects clearly outweigh undesirable effects, or <i>vice versa</i>	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Recommendation can apply to most patients in many circumstances; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak recommendation, high-quality evidence, Grade 2A	Desirable effects closely balanced with undesirable effects	Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies	The best action may differ depending on circumstances or patient or society values; further research is very unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence, Grade 2B	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very	Best action may differ depending on circumstances or patient or society values; higher-quality research may well have an important impact on our confidence in the

Grading Recommendation			
Grade of Recommendation*	Benefit vs. Risk and Burdens	Methodologic Quality of Supporting Evidence	Implications
		strong evidence from observational studies	estimate of effect and may change the estimate
Weak recommendation, low or very low-quality evidence, Grade 2C	Desirable effects closely balanced with undesirable effects	Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable; higher-quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

*The guideline developers use the wording *recommend* for strong (Grade 1) recommendations and *suggest* for weak (Grade 2) recommendations.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients who require treatment with antithrombotic therapy for peripheral artery occlusive disease

POTENTIAL HARMS

- Expected adverse effect of perioperative anticoagulant therapy is an increased risk of wound complications, particularly hematomas.
- An increased risk of major bleeding events has been observed especially with vitamin K antagonists (VKA).
- Side effects of headache, bowel complaints, and palpitations are seen more frequently with cilostazol treatment, compared with placebo. Cilostazol is

- appropriate therapy for patients with moderate to severe disabling claudication who are not candidates for revascularization.
- Higher dose aspirin therapy is more prone to cause side effects and gastrointestinal (GI) complications.
 - Ticlopidine is associated with a substantial risk of leukopenia and thrombocytopenia, requiring close hematological monitoring. Because of these side effects, clopidogrel has replaced ticlopidine as the thienopyridine of choice.

CONTRAINDICATIONS

CONTRAINDICATIONS

Cilostazol is contraindicated in patients with congestive heart failure.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Limitations of These Guideline Development Methods

Limitations of these guidelines include the limited quantity and quality of available studies for some patient groups. Second, it is possible that some authors followed this methodology more closely than others, although the development process was centralized by an evidence-based practice center (EPC) and supervised by the editors. Third, it is possible that the guideline developers missed relevant studies in spite of the comprehensive searching process. Fourth, despite their efforts to begin centralizing the methodologic evaluation of all studies to facilitate uniformity in the validity assessments of the research incorporated into these guidelines, resources were insufficient to conduct this evaluation for all but a few of the recommendations in each chapter. Fifth, the guideline developers performed only few statistical pooling exercises of primary study results. Finally, sparse data on patient preferences and values represent additional limitations inherent to most guideline development methods.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy includes local educational programs and tools offered through the American College of Chest Physicians (ACCP) Board of Governors and select other locations. The Veterans Administration (VA) will also participate in a pilot project.

IMPLEMENTATION TOOLS

Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Sobel M, Verhaeghe R. Antithrombotic therapy for peripheral artery occlusive disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008 Jun;133(6 Suppl):815S-43S. [208 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001 Jan (revised 2008 Jun)

GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Chest Physicians

GUIDELINE COMMITTEE

American College of Chest Physicians (ACCP) Expert Panel on Antithrombotic and Thrombolytic Therapy

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Sobel discloses that he has received grant monies from the National Institutes of Health and the Department of Veterans Affairs.

Professor Verhaeghe discloses that he has received grant monies from Bayer, LEO Pharma, and Sanofi-Aventis.

ENDORSER(S)

American College of Clinical Pharmacy - Medical Specialty Society
American Society of Health-System Pharmacists - Professional Association

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Clagett GP, Sobel M, Jackson MR, Lip GY, Tangelder M, Verhaeghe R. Antithrombotic therapy in peripheral arterial occlusive disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004 Sep;126(3 Suppl):609S-26S.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers of the [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

Executive Summary:

- Antithrombotic and thrombolytic therapy executive summary. Chest 2008 Jun; 133:71S-109S.

Background Articles:

- Antithrombotic and thrombolytic therapy. Chest 2008 Jun; 133:110S-112S.
- Methodology for antithrombotic and thrombolytic therapy guideline development. Chest 2008 Jun; 133:113S-122S.
- Grades of recommendation for antithrombotic agents. Chest 2008 Jun; 133:123S-131S.
- Strategies for incorporating resource allocation and economic considerations. Chest 2008 Jun; 133:132S-140S.

Electronic copies: Available to subscribers of the [Chest - The Cardiopulmonary and Critical Care Journal](#).

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer on September 27, 2001. This NGC summary was updated by ECRI on December 9, 2004. The updated information was verified by the guideline developer on January 12, 2005. This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on March 14, 2008 following the updated FDA advisory on heparin sodium injection. This NGC summary was updated by ECRI Institute on December 2, 2008. The updated information was verified by the guideline developer on January 7, 2009.

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Date Modified: 2/16/2009

